## GW26-e2224

### The Incidence of Atorvastatin-induced Abnormal Liver Function in Chinese Patients: A Systematic Review and Meta-analysis

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**OBJECTIVES** To study the incidence of atorvastatin-induced abnormal liver function in Chinese patients.

**METHODS** Literatures were searched in PubMed, EMBASE, CENTRAL, SinoMed, CMCI, CNKI, VIP and Wanfang database (from their inception to Feb 8, 2015). Randomized controlled trial (RCT), Cohort Study, case series and quasi-experiment studies were included, and generic drugs were excluded. Data extraction and verification were conducted by two reviewers independently. Open Meta-Analyst software with binary random effect model was applied to compute the incidence of atorvastatin-induced abnormal liver function in different doses and periods, and the results were described by rates and 95% confidence intervals (95% CI).

**RESULTS** According to our searching strategy and including criteria, 2386 literatures (2298 Chinese literatures and 88 English ones) published between 2001 and 2015 were included, among which there were 1984 RCT studies, 45 cohort studies, 258 case series studies and 99 quasi-experiment studies. 1140 literatures reported the adverse drug reactions (ADRs) in the process of follow-up, but 1246 literatures did not explicitly mentioned any ADRs. 182430 patients with different diseases such as coronary heart disease, acute coronary syndromes, unstable angina pectoris, hyperlipidemia, atherosclerosis were analyzed. The maximum treatment time was 7 years. Based on the studies reported ADRs (1140 literatures), the numbers of patients in 10mg/d, 20mg/d, 40mg/d and 80mg/d groups were 29079, 54020, 9255 and 1216, respectively, and the corresponding incidence and 95%CI of atorvastatin-induced abnormal liver function were 1.1% (0.9%～1.2%), 1.2% (1.1%～1.3%), 1.3% (1.1%～1.5%) and 2.7% (1.4%～3.9%), respectively. There were no significant differences among different treatment periods in the same dose group. Based on all 2386 literatures, the numbers of patients were 52030, 106009, 18840 and 3352 in four groups, respectively, and corresponding incidence of atorvastatin-induced abnormal liver function were 0.6% (0.5%～0.7%), 0.03% (0.02%～0.05%), 0.6% (0.5%～0.7%) and 0.9% (0.6%～1.2%) with the assume that those studies not mentioned ADRs were the ones with no ADRs. When based on hepatic transaminases > 3 times the upper limit of normal in literatures reported ADRs, the incidence and 95%CI of atorvastatin-induced hepatitis were 0.9% (0.6%～1.1%), 0.9% (0.7%～1.1%), 1.0% (0.6%～1.3%) and 1.4% (0.2%～2.5%) in 10mg/d, 20mg/d, 40mg/d and 80mg/d groups, respectively. In addition, there were 6, 1, 10 and 17 literatures described 5mg/d, 15mg/d, 30mg/d and 60mg/d, respectively, and with few cases of abnormal liver function in each groups (2/566, 1/64, 11/592 and 14/977, respectively).

**CONCLUSIONS** The incidence of atorvastatin-induced abnormal liver function in Chinese patients were very low.

## GW26-e0730

### Effect of phosphocreatine on angiotensininIlinduced proliferation and collagen synthesis in neonatal rat cardiac fibroblasts

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**OBJECTIVES** The aim of this study is to investigate the effect of phosphocreatine (PCr) on angiotensinII(AngII)-induced cardiac fibroblasts in neonatal rats *in vitro* and to clarify its mechanismof action.

**METHODS** The model of myocardial fibrosis induced by AngIIwas established, the effect of phosphocreatine on cultured cardiac fibroblasts(CF) proliferation in the presence or absence of excessive angiotensinII(AngII) was assessed by flow cytometric assay, the area of myocardial collagen was observed by VG staining and the expression of the phosphorylated extracellular signal-regulated kinase (pERK1/2) was detected by immunohistochemistry in each group. The cardiac fibroblasts were randomly divided into four groups: ① the control group ② the AngII group ($1\times10^{-6}$mol/L) ③ the phosphocreatine treated group (10mmol/L) ④ the AngII +phosphocreatine treated group ($1\times10^{-6}$mol/L +10mmol/L).

**RESULTS** The model of myocardial fibrosis was successfully established. Compared to the control group, distribution of CFs in $G_0/G_1$ and $G_2$/M phase in AngIIgroup was decreased ($P<0.01$) with conversely, the increase of the proporation in S phase, the collagen synthesis and the expression of pERK1/2 protein of CFs($P<0.01$). However, no significant difference was observed in cell cycle distribution, collagen synthesis of CFs and the expression of pERK1/2 protein between the control and the phosphocreatine treated group($P>0.05$). Compared to the AngIIgroup, the percentage of CFs in the $G_0/G_1$ phase and $G_2$/M phase was increased with simultaneously, the reduction of S phase and the collagen synthesis in AngII+phosphocreatine treated group ($P<0.01$). Noteworthy, phospho-status of ERK1/2 in the AngII+phosphocreatine treated group demonstrated a higher expression than that in the control group as well as lower than in the AngIIgroup ($P<0.01$).

**CONCLUSIONS** Our study shows that phosphocreatine plays a crucial role in the inhibition of myocardial fibrosis induced by AngIIthrough partially suppressing the CF proliferation and collagen synthesis, which is possibly associated with the inhibition of excessively activated ERK1/2.

## GW26-e1296

### A research on initial dosage of warfarin and target ratio

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**OBJECTIVES** To further acknowledge the optimal initial dosage and offer more reasonable evidence for the application of warfarin in clinical work, the research is adopted by comparing the efficacy and safety of the two dosage regimens to the patients with atrial fibrillation (AF) or pulmonary embolism (PE) by using different initial dosages of warfarin according to the warfarin 3mg and to the BMI.

**METHODS** 81 patients using oral warfarin were randomly assigned to two groups according to different kinds of dosage regimen. The control group included 42 cases started with 3 mg while research group included 39 cases, started with the initial warfarin dosage by the guide of body mass index (BMI) (BMI<25,3mg;25≤BMI<30,4.5mg; BMI≥30,6mg). Follow up one month, to compare the time that INR first stabilized at target range(2.0～3.0), the ratio within stabilized target range at different time, the time that INR stabilized at target range, the times to exceed therapeutic INR (INR>3.0), maintenance dose, and the incidence of bleeding or thrombosis episodes.

**RESULTS** There was no statistical significance between the two groups in baseline characteristics included age, sex, height, weight, BMI, comorbid conditions, drug combination, Baseline INR, left atrial thrombus and pulmonary embolism. Comparing the safety between two groups: there were two cases bleeding slightly in control group and one case in research group, Both groups had no thrombotic events, There was no statistical significance between the two groups (P=1.0). There were no statistical significance between the two groups in the incidence rate to exceed therapeutic INR in different time (P>0.05).There was 7 cases in control group to exceed therapeutic INR at day 15, and 13 cases in research group, There was no statistical significance between the two groups (P=0.082, P>0.05). Comparing the effectiveness between two groups: compared with control group, the ratio to achieve therapeutic INR at day 3, day 5, day 7 were significantly higher in research group ( 38.9% vs. 11.9% at day 3, 51.3% vs. 23.8% at day 5, 71.8% vs. 45.2% at day 7), There was statistical significance between the two groups (P<0.05). Compared with control group, research group required a significantly shorter time to achieve therapeutic INR at the first time (5 days vs. 7 days), There was statistical significance between the two groups (P<0.05). There was no statistical significance between the two groups in the time that INR stabilized therapeutic INR (12 days in research group vs. 15 days in control group), but compared with control group, research group was faster. There was statistical significance between the two groups (P<0.05) in maintenance dose.

**CONCLUSIONS** compared with 3 mg as initial dose, It is more rapid and more effective to achieve therapeutic INR according to body mass index (BMI) guiding the initial warfarin dosage, and bleeding event did not add at the same time.

## GW26-e4473

### Cholesterol in Remnant-Lipoproteins as Measured by Different Methods

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**OBJECTIVES** Elevated remnant-lipoprotein cholesterol (RLP-C) levels are associated with an increased risk of ischemic heart disease. The concurrence of RLP-C measurement by different separation methods is not well-described. This analysis assessed RLP-C by 3 commonly used measurements including immunoseparation (IM [ApoA-I and ApoB-100 monoclonal antibodies]), vertical auto profile (VAP [IDL+$VLDL_3$]) and Calculated RLP-C (Total cholesterol minus HDL-C minus LDL-C) methods using samples from a previously reported randomized, clinical trial.

**METHODS** This analysis assessed fasting RLP-C in hyperlipidemic patients (n=2,382) treated with ezetimibe/simvastatin (E/S)10/20 mg, E/S + niacin (N) 2g and N 2g during 24 weeks, and E/S 10/20 mg and E/S + N 2g during 64 weeks. RLP-C levels, change from baseline and % change from baseline were evaluated by the IM, VAP, and Calculated methods. The relationships and agreement among the 3 methods used in the measurement of these parameters were assessed by Pearson correlation coefficients and Bland-Altman, respectively.

**RESULTS** Cholesterol mass at baseline measured by the VAP and Calculated methods was ~3-4X higher than by IM; all declined with treatment by 24 weeks with little further reduction at 64 weeks (see table). RLP-C change and % reduction from baseline were larger when measured by VAP versus Calculated and IM methods. Although the 3 methods were moderately to strongly correlated (r=0.37-0.79) for RLP-C levels and changes, Bland-Altman plots showed little agreement between the methods for RLP-C levels but slightly better agreement for RLP-C changes (not shown).

**CONCLUSIONS** RLP-C defined by IM, VAP and Calculated methods differs in mass and response to pharmacologic intervention. Given the relationship between RLP-C and IHD risk, standardization of methods is needed for RLP-C use in risk assessment.

## GW26-e2366

### Changes in Carotid Plaque Lipid Content in Subjects Who Continued and Discontinued Statin Therapy

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**OBJECTIVES** Changes in carotid plaque lipid-rich necrotic core (LRNC) as assessed by magnetic resonance imaging (MRI) were investigated in subjects who continued and discontinued statin therapy for 2 years after a prospective study.

**METHODS** The Rosuvastatin Evaluation of Atherosclerotic Chinese Patients (REACH) study in 32 lipid treatment naïve subjects with LRNC showed a significant reduction in LRNC during 24 months (M) of rosuvastatin therapy. All subjects received a clinical follow-up (F/U) visit and a repeat carotid MRI scan at 48 M as planned REACH-F/U. Despite receiving a strong recommendation to continue the statin therapy at 24 M when REACH was completed, only 15 subjects continued taking statins (rosuva.=9, simva.=4 and atorva.=2) in REACH-F/U and 17 discontinued. Lipids and LRNC, both in volume (V) and % (LRNC-V/Wall V×100%), were compared between the statin-continued and -discontinued groups at 48 M.

**RESULTS** There were no significant differences in demographic, clinical characteristics, lipids and plaque changes during 24 M in REACH between the statin-continued and -discontinued groups in REACH-F/U. Not surprisingly, at 48 M, Total-Cholesterol (C), LDL-C and triglycerides were significantly lower in subjects who continued statin than those discontinued (163±43 vs. 207±30 mg/dl, p=0.002), (93±36 vs. 131±22 mg/dl, p=0.001) and (85±27 vs. 143±65 mg/dl, p=0.003), while HDL-C levels were similar. LRNC-V and %LRNC decreased significantly from 24 M in the statin-continued group (101±76 $mm^3$ at 24 M vs. 76±65 $mm^3$ at 48 M, p=0.001) and (17.3±11.9% at 24 M vs. 12.6±7.6% at 48 M, p=0.04). By contrast, subjects who discontinued statin showed non-statistically significant increase in LRNC-V and %LRNC (103±93 $mm^3$ at 24 M vs. 112±106 $mm^3$ at 48 M, p=0.4) and (15.4±11.3% at 24 Mvs. 16.7±11.4% at 48 M, p=0.07). Furthermore, the changes in LRNC-V and %LRNC from 24 to 48 M were significantly different between the statin-continued and -discontinued groups in REACH-F/U (-25±18 vs. 9±14 $mm^3$, p<0.001) and (-4.6± 8.2% vs. 1.3±2.8%, p=0.009).

**CONCLUSIONS** Continued statin therapy leads to continued decrease in LRNC, which indicates improved plaque stability. The REACH-F/U results provided vascular biological evidence to strongly support long-term statin therapy.

## GW26-e3950

### Uninterrupted Dabigatran versus Warfarin in the Treatment of Intracardiac Thrombus in Patients with non-Valvular Atrial Fibrillation

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**OBJECTIVES** The oral direct thrombin inhibitor dabigatran has a predictable anticoagulant effect and may be an alternative medication to warfarin for non-valvular atrial fibrillation (AF) patients with intracardiac thrombus. The objective is to compare the dabigatran, administered at a fixed dose of 150 mg twice daily (bid) with dose-adjusted warfarin (with a target international normalized ratio INR level of 2.0 to 3.0).

**METHODS** In the trial, 41 patients who had intracardiac thrombus detected by transesophageal echocardiography (TEE) were enrolled. Among them, 19 patients received dabigatran 150 mg bid and the remaining 22 patients received warfarin based on the patients' individual choice. Repeated TEE was performed at 3 months. The patients was assessed after 1 month and then 3 months in the clinic; meanwhile they were requested to contact the investigator immediately if symptoms developed that were suggestive of stroke, thromboembolism or major bleeding. All statistical analyses were conducted with SPSS Statistics version 17.0 software. The thrombus dissolution ability, represented by the ratio of decreased thrombus area to original area, was compared by Wilcoxon W test between the 2 groups. Difference with p value < 0.05 (2-sided) was considered statistically significant.

**RESULTS** Mean age of the study population was 57.7±7.4 years, with 36 (87.8%) male and 17 (41.5%) patients who had persistent AF, with no differences between the 2 groups. Thrombus area ranges from 0.1 to 4.48 $cm^2$ and the locations of thrombi were mainly in left atrial appendage (LAA). The thrombus area in warfarin group were larger than in dabigatran group (1.45±1.04 vs. 0.64±0.54, p < 0.05). Mean number of INR examination values obtained in the warfarin group was 10 during the therapy course. Time in therapeutic range of INR (TTR) was above 60%. Complete thrombus resolution was documented by repeated TEE in 17 patients in dabigatran group (17 of 19) and 17 patients in warfarin group (17 of 22). The ability of thrombus dissolution, represented by the ratio of decreased thrombus area to original area, was similar between the 2 groups (p > 0.05). Any bleeding, occurred in 7 patients receiving dabigatran and in 8 patients receiving warfarin. No major or fatal bleeding occurred in both two groups. One patient in the warfarin group experienced ischemic stroke. Four patients in the dabigatran group had gastrointestinal discomfort. Only one patient discontinued dabigatran for about two weeks and needed drug intervention, and after 3-month anticoagulation, a secondary TEE detected an increased thrombus.

**CONCLUSIONS** Dabigatran has similar effect compared with warfarin for the treatment of intracardiac thrombus in patients with non-valvular AF. Uninterrupted dabigatran is particularly essential and crucial for fibrinolysis and drug discontinuance would affect thrombus dissolution effect. It should be noticed that dabigatran lead to gastrointestinal discomfort event.

## GW26-e0675

### Comparison of Ticagrelor with Clopidogrel in the Treatment of Patients with Acute Coronary Syndrome in Platelet Reactivity

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**OBJECTIVES** To compare the inhibitory effect of ticagrelor and clopidogrel on the platelet of patients with acute coronary syndrome(ACS) after percutaneous coronary artery intervention(PCI).

**METHODS** 255 cases of patients with ACS admitted in our hospital from March 2014 to August 2014 were selected for this study, in which 85 cases were treated by ticagrelor and aspirin and the other 170 cases were treated by clopidogrel and aspirin respectively. All the patients were given PCI treatment, and the thrombelastography(TEG) were detected 2 days after PCI and oral administration of load dosage of antiplatelet drugs, the platelet inhibition ratio through ADP and AA pathway were observed and compared between two groups.

**RESULTS** Adenosine diphosphate(ADP)-induced platelet inhibition ratio in clopidogrel group was significantly lower than that of in ticagrelor group (66.60±25.57% vs 82.10±18.87%, P<0.05). Arachidonic acid(AA)-induced platelet inhibition ratio in clopidgrel was similar to that of in ticagrelor group (88.70±23.89% vs 90.32±18.09%, P>0.05). There were significant differences between clopidogrel